Complete Summary

GUIDELINE TITLE

Membranous nephropathy: role of alkylating agents.

BIBLIOGRAPHIC SOURCE(S)

Thomas M. Membranous nephropathy: role of alkylating agents. Nephrology 2006 Apr;11(S1):S154-61.

Thomas M. Membranous nephropathy: role of alkylating agents. Westmead NSW (Australia): CARI - Caring for Australasians with Renal Impairment; 2005 Sep. 16 p. [22 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Membranous nephropathy

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine

Nephrology
Pediatrics

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the available clinical evidence pertaining to the impact of alkylating agents on renal functional decline in membranous glomerulonephritis with poor prognostic features, such as heavy proteinuria (>3 g/24 h), impaired renal function at presentation, deteriorating renal function and/or reduced response to therapy

TARGET POPULATION

Adults and children with nephrotic syndrome and idiopathic membranous nephropathy

INTERVENTIONS AND PRACTICES CONSIDERED

Alkylating agents

MAJOR OUTCOMES CONSIDERED

Rate of remission

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Databases searched: MeSH terms and text words for Membranous Nephropathy were combined with MeSH terms and text words for alkylating agents. This search was carried out in Medline (1966 to September Week 1 2004). The Cochrane Renal Group Trials Register was also searched for trials of membranous nephropathy not indexed in Medline.

Date of searches: 9 September 2004.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level I: Evidence obtained from a systematic review of all relevant randomized controlled trials (RCTs)

Level II: Evidence obtained from at least one properly designed RCT

Level III: Evidence obtained from well-designed pseudo-randomized controlled trials (alternate allocation or some other method); comparative studies with concurrent controls and allocation not randomized, cohort studies, case-control studies, interrupted time series with a control group; comparative studies with historical control, two or more single arm studies, interrupted time series without a parallel control group

Level IV: Evidence obtained from case series, either post-test or pretest/post-test

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Recommendations of Others. Recommendations regarding the role of alkylating agents in membranous nephropathy from the following groups were discussed: Kidney Disease Outcomes Quality Initiative, UK Renal Association, Canadian Society of Nephrology, European Best Practice Guidelines, and International Guidelines.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the levels of evidence (I–IV) can be found at the end of the "Major Recommendations" field.

Guidelines

a. Treatment with alkylating agents is associated with an increased rate of remission in patients with nephrotic syndrome and idiopathic membranous nephropathy when compared to steroid therapy alone or no therapy. (Level I evidence)
b. There is insufficient data to confirm that this effect translates into an improvement in renal outcomes. (Level I evidence)

Suggestions for Clinical Care

(Suggestions are based on Level III and IV evidence)

Who to Treat?

- To avoid possibly unnecessary treatments and toxicity, most clinical studies have focused on individuals who are thought to be at risk for progressive disease. Consequently, at this time, the clinical use of alkylating agents in membranous nephropathy should be restricted to individuals with poor prognostic features, such as heavy proteinuria (> 3 g/24 h), impaired renal function at presentation, deteriorating renal function and/or reduced response to supportive therapy.
- A variety of models incorporating a range of clinical and histological features have been validated, with the ability to predict the development of chronic renal insufficiency of up to 86%, with a sensitivity of more than 60%. Such a model could be used to target therapy by identifying individual patients at risk for progressive disease. Treatment algorithms based on these models have been proposed. These have not been tested in large-scale trials.
- Currently, there is no evidence to support disease-specific intervention in adult patients with good prognostic features (proteinuria < 3 g/day and normal renal function), although supportive therapy including aggressive

control of blood pressure and dyslipidemia and blockade of the rennin angiotensin system would seem prudent. (Level IV evidence) Nonetheless, long-term follow-up is still required to monitor for the development of adverse indicators to identify additional patients at risk for progressive kidney disease. (Level IV evidence)

When to Treat

- The possibility of spontaneous remission has led many authors to suggest that a 6-month period on conservative therapy (including aggressive control of blood pressure and dyslipidemia and blockade of the renin angiotensin system) may be valuable before embarking on cytotoxic therapy. (Level IV evidence)
- While most studies have dealt with early treatment of patients with adverse prognostic features (and excluded patients with established renal impairment) there have been a few small studies to suggest that even late intervention may be efficacious. (Level III evidence)
- Although such studies imply that a brief delay may not be harmful, the progression of control patients over a short period in many of the trials described below should mean this course should only be conducted with cautious observation. (level IV evidence)

Definitions:

Levels of Evidence

Level I: Evidence obtained from a systematic review of all relevant randomized controlled trials (RCTs)

Level II: Evidence obtained from at least one properly designed RCT

Level III: Evidence obtained from well-designed pseudo-randomized controlled trials (alternate allocation or some other method); comparative studies with concurrent controls and allocation not randomized, cohort studies, case-control studies, interrupted time series with a control group; comparative studies with historical control, two or more single arm studies, interrupted time series without a parallel control group

Level IV: Evidence obtained from case series, either post-test or pretest/post-test

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of alkylating agents in patients with membranous glomerulonephritis

POTENTIAL HARMS

To avoid possibly unnecessary treatments and toxicity, at this time, the clinical use of alkylating agents in membranous nephropathy should be restricted to individuals with poor prognostic features, such as heavy proteinuria (> 3 g/24 h), impaired renal function at presentation, deteriorating renal function and/or reduced response to supportive therapy.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Sep

GUIDELINE DEVELOPER(S)

Caring for Australasians with Renal Impairment - Disease Specific Society

SOURCE(S) OF FUNDING

Industry-sponsored funding administered through Kidney Health Australia

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Author: Merlin Thomas

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All guideline writers are required to fill out a declaration of conflict of interest.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Caring for Australasians with Renal Impairment Web site.

Print copies: Available from Caring for Australasians with Renal Impairment, Locked Bag 4001, Centre for Kidney Research, Westmead NSW, Australia 2145

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- The CARI guidelines. A guide for writers. Caring for Australasians with Renal Impairment. 2006 May. 6 p.

Electronic copies: Available from the Caring for Australasians with Renal Impairment (CARI) Web site.

PATIENT RESOURCES

None available

NGC STATUS

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